REMARKS

Claims 1-6 and 8-24 appear in this application for the Examiner's review and consideration. This response is in addition to applicants prior response to the final office action.

In the Advisory Action, the Examiner states that a side-by-side study of the compound of U.S. Patent No. 5,284,867 to Kloog et al. ("Kloog") and the compound of the present invention should be submitted to support Applicants' assertion that Kloog's HU-211 and the HU-211 claimed are significantly different compounds with different properties, which are attributable to the differences in enantiomeric purity. Kloog reports that the inventors discovered that HU-211 at about 25 mg/kg per body weight, administered most likely to mice, induced stereotypy, locomotor hyperactivity and tachycardia (Col. 5, lines 26-32). In contrast, the compound of the present invention was administered at single doses of 50 mg/kg in rats, 25 mg/kg in rabbits and 50 mg/kg in monkeys, with no observed adverse effects (Specification at page 33, lines 26-28). The present compounds can be administered advantageously at higher doses, without causing deleterious side effects. A Declaration of Avihai Yacovan, presenting the results of a side-by-side study, is submitted with this amendment. Applicants submit the results of the study below.

Initially, Applicants note that samples of Kloog's HU-211 are no longer available to them (Yacovan Declaration, ¶ 5). To obtain the closest comparable samples, a laboratory scale batch of HU-211 was prepared according to a slightly improved version of Mechoulam's original synthetic procedure ("Mechoulam sample") (*Id.*). This batch was tested and found to contain 91.1% HU-211 and 0.26% HU-210, yielding an enantiomeric excess of 99.4% (*Id.*), which is less than the at least 99.90% claimed. These values represent the best values that could have been obtained by Kloog (*Id.*). HU-211 was also prepared according to the disclosure in the pending application ("Ultrapure sample") (*Id.* at ¶ 6).

Three of the four parameters usually tested in the mice tetrad assay were performed on ICR male mice (*Id.* at ¶ 7). The animals were administered the Mechoulam or Ultrapure sample intravenously at a dose of 50 mg/kg and at a volume dose of 5 mL/kg (*Id.*). Untreated animals and animals injected with only the vehicle served as controls (*Id.*). Measurements evaluating suppression of spontaneous activity, hypothermia, and catalepsy were taken (*Id.*). The results of the tests are provided in the table below (*Id.* at ¶ 8):

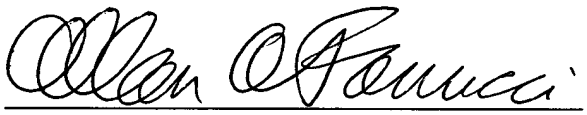
Treatment	Rectal Temperature (°C)	Spontaneous Locomotion (No. of Squares)	Catalepsy (Sec)
Untreated (Control)	38.78 ± 0.18	74.51 ± 9.96	0.00 ± 0.00
Ultrapure	38.48 ± 0.12	86.58 ± 13.12	0.00 ± 0.00
Mechoulam	32.96 ± 0.25	4.42 ± 3.13	29.40 ± 8.69

The results show that the Mechoulam sample clearly produces adverse effects, while the Ultrapure sample does not (*Id.* at ¶ 9). For example, the Mechoulam sample caused a drastic drop in rectal temperature, almost totally inhibited spontaneous locomotion, and caused significant catalepsy (*Id.*). Thus, it can be inferred from the results that Kloog's HU-211 and the HU-211 claimed are significantly different compounds with different properties.

Accordingly, Applicants believe that the application is now in condition for allowance, early notice of which would be appreciated. Should any issues remain, the Examiner is invited to contact the undersigned attorney of record in an effort to expedite the processing of this application.

Respectfully submitted,

Date: 9/14/05



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